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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/737,319	11/12/1996	SUSUMU KAJIWARA	081356/011	5074

7590 10/28/2003

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EXAMINER	
KERR, KATHLEEN M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 10/28/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/737,319	KAJIWARA ET AL.	
	Examiner	Art Unit	
	Kathleen M Kerr	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9 and 12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Application Status

1. In response to the previous Office action, a non-Final rejection (Paper No. 18, mailed on April 24, 2003), Applicants filed a response and amendment received on August 7, 2003 (Paper No. 20). Said amendment cancelled Claims 6-8 and 10-11, amended Claim 9, and added new Claim 12. Thus, Claims 9 and 12 are pending in the instant Office action and will be examined herein.

Priority

2. As previously noted, the instant application is granted the benefit of priority for the foreign application 51234/1995 filed in Japan on March 10, 1995. Receipt is acknowledged of papers submitted under 35 U.S.C. § 119(a)-(d), which papers have been placed of record in the file. A translation of said foreign application was filed on June 13, 2003; said application discloses the claimed invention. Thus, for purposes of the instant Office action, the effective filing date of the pending claims is March 10, 1995.

Drawings

3. Drawings filed on August 7, 2003 have been approved by the Draftsmen and are, therefore, entered as formal drawings acceptable for publication upon the identification of allowable subject matter.

Withdrawn - Objections to the Specification

4. Previous objection to the Abstract for not completely describing the disclosed subject matter is withdrawn by virtue of Applicants' amendment.

Maintained - Objections to the Specification

5. Previous objection to the specification because the title is not descriptive is maintained. While Applicants amended the title to the title proposed by the Examiner, Applicants also amended the claims deleting claims to the DNA products. Thus, the proposed title is not longer descriptive of the claimed invention. A new title is required that is clearly indicative of the invention to which the elected claims are drawn (see M.P.E.P. § 606.01). The Examiner suggests the following new title:

--- Methods of Producing Carotenoids Using DNA Molecules encoding Isopentenyl Pyrophosphate Isomerase---

Withdrawn - Objections to the Claims

6. Previous objection to Claims 9 and 10 for improper English is withdrawn by virtue of Applicants' amendment and/or cancellation of said claims.

7. Previous objection to Claim 11 for a typographical error is withdrawn by virtue of Applicants' cancellation of said claims.

New or Maintained - Claim Rejections - 35 U.S.C. § 112

8. Previous rejection of Claim 9 under 35 U.S.C. § 112, first paragraph, written description, is maintained. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicants argue that the "at least three different DNA sequences encoding IPP isomerase" constitute a "representative number" of species to adequately describe the genus of methods claimed. The Examiner disagrees. At the time of the invention, few IPP isomerase genes were known and no investigations of structure/function have been taught. Thus, the Examiner maintains that one of skill in the art would be unable to predict the structure of the other members of the claimed genus of DNA sequences used in the methods.

Applicants also argue that a teaching of three sequences along with a disclosure of "substantial homology" to said sequences defines the structural features of the genus; the Examiner disagrees. To define the structural features that support IPP isomerase activity, mutagenesis or at least consensus sequence studies would be required to identify conserved, if not required, residues. Applicants further argue that the genus of DNA molecules hybridizing to the disclosed sequences also aids the skilled artisan in assessing the structure of the genus. The Examiner disagrees because no description of required structure to retain IPP isomerase activity is found in the specification and/or the prior art. Thus, the field is not developed enough to support a skilled artisan recognizing a structure by function alone, as is the case for Claim 9.

9. (New) Claims 9-10 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The abbreviation "IPP" in line 3 of Claim 9 is used in the claims without definition. The Examiner suggests replacing the abbreviation with ---IPP (isopentenyl pyrophosphate)--- for clarity.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 9 and 12 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Yamano *et al.* (see IDS Paper No. 2) in view of Anderson *et al.* (see IDS Paper No. 2) and in view of Albrecht *et al.* (Light-Stimulated Carotenoid Biosynthesis during Transformation of Maize Etioplasts Is Regulated by Increased Activity of Isopentenyl Pyrophosphate Isomerase. Plant Physiology (1994) 105:529-534). The instant claims are drawn to methods of making carotenoids in a carotenoid-producing microorganism by introducing a DNA that encodes *S. cerevisiae* IPP isomerase (SEQ ID NO:3).

Yamano *et al.* teach the metabolic engineering of *S. cerevisiae* to make carotenoids by introducing crtE, -B, -I, and -Y genes and culturing the yeast to produce carotenoids (see Abstract, page 1113 and Table). Yamano *et al.* also teach that IPP, DMAPP, GPP and GGPP are

precursors in the biosynthesis of carotenoids (see page 1112 and Figure 1) and using yeast to produce commercial quantities of carotenoids (see page 1114, right column). Despite the well-known usefulness of excess precursor supply in the up-regulation of biosynthetic pathways in microorganisms, Yamano *et al.* do not teach the simultaneous introduction of IPP isomerase to produce more IPP and/or DMAPP in the engineered *S. cerevisiae*.

Anderson *et al.* teach the IPP isomerase gene from *S. cerevisiae* (see title).

Albrecht *et al.* teach that increased carotenoid biosynthesis is accompanied by increased IPP isomerase activity (see Abstract).

It would have been obvious to one of skill in the art to combine the above teachings and practice a method of making carotenoids using the engineered cells of Yamano *et al.* with the addition of the IPP isomerase gene from *S. cerevisiae* taught by Anderson *et al.* because the overproduction of early precursors of biosynthetic pathways is well-known in the art to help increase production of the product of the pathway. Anderson *et al.* provided the ideal gene for overproduction, that of IPP isomerase of the endogenous host cell, *S. cerevisiae*; its ideality is identified by Albrecht *et al.* who teach a link between increased IPP isomerase activity and increased carotenoid production. One would have been motivated to practice the invention because of the commercial usefulness of carotenoids such as β-carotene and lycopene when produced in large quantities by microorganisms such as yeast. One would have had a reasonable expectation of success that the introduction of the IPP isomerase gene (Anderson *et al.*) into the engineered *S. cerevisiae* cells (Yamano *et al.*) could be accomplished easily because said gene is endogenous to said engineered cells.

Summary of Pending Issues

11. The following is a summary of the issues pending in the instant application:

a) The specification stands objected to because the title is not descriptive.

b) Claim 9 stands rejected under 35 U.S.C. § 112, first paragraph, written description.

c) Claims 9-10 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the abbreviation "IPP".

d) Claims 9 and 12 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Yamano *et al.* in view of Anderson *et al.* and in view of Albrecht *et al.*

Allowable Subject Matter

12. As previously noted, the *P. rhodozyma* and H. *pluvialis* IPP isomerase genes are free of the prior art. Thus, methods of producing carotenoids using DNA encoding SEQ ID NOs: 1 or 2 are also free of the prior art.

Conclusion

13. Claims 9 and 12 are rejected for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution. The instant Office action is **non-final** based on the new ground of rejection, the art rejection under 35 U.S.C. § 103(a).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

KMK
October 24, 2003